REMARKS

The foregoing amendment and following remarks are in response to the Office Action, mailed October 1, 2010. Reconsideration and continued examination of the above-referenced patent application is respectfully requested.

Claims 1-4, 6-8, 10-17, and 19-23 are pending. Claims 1-4, 7, 10, 14, 15, 17, and 19 have been amended. Claim 6 has been cancelled. New claims 22 and 23 have been added. Support for claim amendments and new claims may be found at, for example, paragraphs 19, 34, 49-51, 53, and 61 of U.S. Patent Application Publication No. 2006/0286138 corresponding to the present application. No new matter has been introduced.

Claims 1-4, 6-8, 10-17, and 19-21 stand rejected. Claims 1-3, 6, 11, and 19 stand rejected under 35 U.S.C. §103(a) as being obvious given U.S. Patent Application Publication No. 2003/0208259 to Penhasi ("Penhasi"). Claims 1, 3, 4, 8, 10, 12, 15, and 17 stand rejected under 35 U.S.C. §103(a) as being obvious given U.S. Patent Application Publication No. 2003/0211035 to Burns et al. ("Burns"). Claim 16 stands rejected under 35 U.S.C. §103(a) as being obvious given Burns in view of a combination of "Journal of Controlled Release 1991, 16:341-348" by Yoshioka et al. ("Yoshioka") and "Biodegradation 2002, 13:141-147" by Hoshino et al. ("Hoshino"). Claims 1, 3, 4, 8, 12-14, 17, 20, and 21 stand rejected under 35 U.S.C. §103(a) as being obvious given U.S. Patent No. 5,635,216 to Thompson et al. ("Thompson") in view of U.S. Patent No. 6,562,939 to Farachi et al. ("Farachi"). Claims 1 and 7 stand rejected under 35 U.S.C. §103(a) as being obvious given International Publication No. WO 94/21228 to Duan et al. ("Duan") in view of a combination

of U.S. Patent No. 4,524,191 to Nakamura et al. ("Nakamura") and Burns. These rejections are respectfully traversed.

In view of the following remarks, it is submitted that the claims pending in the application are novel and nonobvious and that the rejections are traversed. It is believed that this application is in condition for allowance. By this response, reconsideration of the present application is respectfully requested.

The Examiner is reminded that to successfully make a *prima facie* rejection under 35 USC § 103, the Examiner must show that Assignee's claimed subject matter would have been obvious to one of ordinary skill in the art pertinent to Assignee's claimed subject matter at the time it was made. *See*, KSR International, Co. v. Teleflex, Inc., US Supreme Court (decided April 30, 2007). Some of the factors to consider in this analysis include the differences between the applied documents and Assignee's claimed subject matter, along with the level of skill associated with one of ordinary skill in the art pertinent to Assignee's claimed subject matter at the time it was made. One way in which an Examiner may establish a *prima facie* case of unpatentability under 35 USC § 103 would be to show that three basic criteria have been met. First, the Examiner should show that the applied documents, alone or in combination, disclose or suggest every element of Assignee's claimed subject matter. Second, the Examiner should show that there is a reasonable expectation of success from the proposed combination. Finally, the Examiner should show that there was some suggestion or motivation, either in the applied documents themselves or in the knowledge generally available to one of ordinary skill in the art pertinent to the claimed subject matter at the relevant time, to modify the document(s) or to combine

document teachings. The motivation or suggestion to make the proposed combination and the reasonable expectation of success should be found in the prior art, and should not be based on Assignee's disclosure. *See*, In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *See*, MPEP § 2142; 2143 - § 2143.03 (regarding decisions pertinent to each of these criteria). It is respectfully asserted that the Examiner has not met these standards.

Furthermore, on October 10, 2007, the USPTO published in the Federal Register its Examination Guidelines under 35 USC § 103 in view of the KSR decision, cited above. These guidelines contain a number of relevant points. In particular, the new Guidelines state that an Examiner must articulate a reason or rationale to support an obviousness rejection. Specifically, Examiner's must articulate findings as to the scope and content of the prior art to support the obviousness rejection being made. The Examiner should focus on the state of the art and not on impermissible hindsight (e.g., from inappropriate use of Assignee's disclosure). Specifically, Examiners need to account for all claim limitations in the rejections, either by indicating how each limitation is shown by the applied documents or by providing an explanation of how the document is legally relevant despite the limitation not being shown. Thus, Examiners must explain reasoning that provides a nexus between the factual findings and the legal conclusions of obviousness. Recently, the USPTO has published 2010 KSR Guidelines Update in the Federal Register at Vol. 75, No. 169, Pp. 53643 – 53660. The 2010 KSR Guidelines Update also require the Examiner to articulate findings as to the scope and content of the prior art to support the obviousness rejection being made.

It is respectfully asserted, however, that not every limitation of the rejected claims is found in the documents applied by the Examiner and that the proposed combination is not proper, as the Examiner has not met the standards discussed above.

Claims 1-3, 6,11, and 19 - Penhasi

Claims 1-3, 6, 11, and 19 stand rejected under 35 U.S.C. §103(a) as being obvious given Penhasi. The Examiner stated that Penhasi "teaches catheters, surgical mesh and films structures for their devices composed of a blend of elastomeric and non-elastomeric polymers along with a drug." [Office Action, P. 3.] The Examiner further states that Penhasi shows that the drug is incorporated in a polymer matrix. [Office Action, P.4.] The Examiner acknowledged that Penhasi "does not provide an explicit example where polyethelene sebacate is the non-elastomeric polymer in the blend." [Office Action, P. 4.] However, the Examiner stated that it would have been obvious to one or ordinary skill in the art at the time of the invention to select polyethylene sebacate as the non-elastomeric polymer for a drug/polymer blend. [Office Action, Pp. 4-5.] The Examiner further stated that "molded" in claim language "non-stent molded implant" of claim 1 is a product-by-process limitation that confers no additional structural limitations to the implant. [Office Action, P. 4.]

Assignee disagrees with the Examiner's argument that the claim language, "non-stent molded implants," recited in claim 1 is a product-by-process limitation and notes that a person of skill in the art would readily distinguish between a molded implant and an implant that is not molded. However, to expedite prosecution, Assignee has amended claim 1 to delete the word "molded" from "non-stent molded implant." Assignee has similarly

amended "coated granules" and "coated tablets" to remove "coated" from the claim language. Accordingly, Assignee therefore submits that claim 1 does not contain product-by-process language.

Claim 1, as amended, recites (with emphasis added):

> 1. A pharmaceutical composition, comprising:
> at least one pharmaceutically active ingredient;
> **poly(ethylene sebacate)**; and
> wherein said pharmaceutical composition comprises one or more solid or liquid drug delivery systems, wherein said one or more solid or liquid drug delivery systems comprise one or more of the following structures: drug loaded microparticles, microcapsules, nanoparticles, non-stent molded implants, coated granules, films, coated tablets, ophthalmic inserts, fibers, ligatures or sutures.

Assignee disagrees with the Examiner that it would have been obvious to select poly(ethelene sebacate) as a non-elastomeric polymer in a pharmaceutical composition. Penhasi appears to show examples in which only a *polylactide* ("PLA"), such as poly(DL-lactide) is used as a non-elastomeric polymer in a polymer blend. [Para. 34.] Assignee notes that the use of *poly(ethelene sebacate)* instead of PLA provides numerous unobvious and unexpected benefits.

The 2010 KSR Guidelines Update provides an analogous example where a combination of materials shown in different documents was determined to be improper. Example 4.18, e.g., refers to Sanofi-Synthelabo v. Apotex, Inc. 550 F.3d 1075 (Fed. Cir. 2008), finding that "[a] claimed stereoisomer would not have been obvious where the claimed stereoisomer exhibited unexpectedly strong therapeutic advantages over the prior art racemic mixture without the correspondingly expected toxicity, and the resulting properties of the enantiomers separated from the racemic mixture were unpredictable." [Fed. Reg., Vol. 75, No. 169, P. 53655.] Assignee notes that Example 4.18 is analogous

because the use of *poly(ethelene sebacate)* instead of PLA, as shown in Penhasi, provides numerous unexpected and unpredictable advantages over PLA, as discussed below.

For example, Assignee notes that the chemical compatibility of pharmaceutical compositions, e.g., medicines, having poly(ethylene sebacate) is superior to that of the PLA and Polyglycolide ("PGA") compositions of Penhasi due to a lower polarity and a greater solubility. Moreover, pharmaceutical compositions, e.g., medicines, having *poly(ethylene sebacate)* may also provide numerous other advantages over PLA and PGA compositions, such as a lower melting point and lower viscosity to allow solvent-free process, loading and excellent control over drug release.

Additional advantages of poly(ethylene sebacate) are that it is *hydrolytically stable* and is capable of *degrading to release a water-insoluble acid*. Assignee notes that biodegradable polymers such as PLA and PGA have a relatively high ester group concentration as a result of a lower molecular weight of polymerizing units, and are therefore not *hydrolytically stable*. Use of poly(ethylene sebacate) that is *hydrolytically stable* is advantageous because it is not affected by the presence of water around a drug delivery system. Moreover, Penhasi does not appear to show that the PLA shown in Penhasi is capable of degrading to release a water-insoluble acid, as the poly(ethylene sebacate) recited in claim 1 is capable of doing.

Claim 1 therefore distinguishes Penhasi. Claims 2-4, 6-8, 10-17, 19, 22, and 23 depend, directly or indirectly (e.g., through claim dependencies) from claim 1 and therefore also distinguish Penhasi for at least the same reasons as those discussed above with respect to claim 1.

Claims 1, 3-4, 8, 10, 12, 15, and 17 - Burns

Claims 1, 3-4, 8, 10, 12-15, and 17 stand rejected under 35 U.S.C. §103(a) as being obvious given Burns. The Examiner states that Burns shows "microspheres composed of polymers that are envisioned for biomedical applications." [Office Action, P. 6.] The Examiner also states that Burns shows microparticles "envisioned for controlled (sustained) release" and that the microparticles are suspended in gel. The Examiner further states that it would have been obvious to a person of ordinary skill in the art at the time of the invention to utilize polyethylene sebacate in bioactive microparticles. [Office Action, P. 7]

Burns appears to show a method of forming polymeric microspheres for biomedical applications. [Abstract] However, as acknowledged by the Examiner, Burns does not show that the microspheres would include *poly(ethylene sebacate)*.

As discussed above, poly(ethylene sebacate) provides numerous unexpected and unpredictable advantages over other biodegradable polymers such as PLA and PGA. For example, poly(ethylene sebacate) is *hydrolytically stable* and is capable of degrading to *release a water-insoluble acid*. Burns does not appear to show use of any hydrolytically stable material or the release of any *water-insoluble acid* upon degradation of poly(ethylene sebacate) or any other polymer.

Claim 1 therefore distinguishes Burns. Claims 2-4, 6-8, 10-17, 19, 22, and 23 depend, directly or indirectly (e.g., through claim dependencies) from claim 1 and therefore also distinguish Burns for at least the same reasons as those discussed above with respect to claim 1.

Claim 16 – Burns in view of Yoshioka and Hoshino

Claim 16 stand rejected under 35 U.S.C. §103(a) as being obvious given Burns in view of a combination of Yoshioka and Hoshino. The Examiner states that Burns makes obvious nanoparticles compose of linear aliphatic polyester, but does not show the presence of a lipase in the microparticles. [Office Action, P. 7.] However, the Examiner states that Yoshioka shows the inclusion of an agent in a polymeric drug delivery system to hydrolyze the polymer and allow control of degradation rate of the polymer and subsequent rate of drug release. [Office Action, P. 8.] The Examiner also states that Hoshino shows that lipases were known to degrade a linear aliphatic polyester of the same form as polyethylene sebacate. [Office Action, P. 8.] That Examiner further states that it would have been obvious to a person of ordinary skill in the art at the time of the invention to combine Burns with Yoshioka and Hoshino in the direction of claim 16.

Assignee notes that claim 16 depends from claim 1 and therefore distinguishes Burns for at least the same reasons as those discussed above. Yoshioka and Hoshino do not make up for the deficiencies of Burns. Yoshioka and Hoshino both appear to show studies of biodegradable systems. Yoshioka appears to show a study of polymer hydrolysis in base-loaded poly films.

Claim 16 recites "*drug delivery systems comprise lipase* capable of modifying release of said pharmaceutically active ingredient."

However, Yoshioka does not show use of a lipase in the study. [Yoshioka, P. 341.] Hoshino appears to show a study of lipases for their degradation efficiency of aliphatic polyester films, such as poly (L-lactide) (PLA). [Hoshino, Abstract.] Assignee notes that claim 1, from which claim 16 depends, recites use of *poly(ethylene sebacate)*, not *PLA*.

Moreover, paragraph 18 of the present application distinguishes PLA, listing disadvantages of PLA polyesters.

Neither Yoshioka nor Hoshino, alone or in combination with Burns, show use of poly(ethylene sebacate) or any other polymer that that has advantages such as being *hydrolytically stable* or capable of degrading to *release a water-insoluble acid*. Accordingly, claim 16 therefore distinguishes Burns in view of Yoshioka and Hoshino .

Claims 1, 3, 4, 8, 12-14, 17, 20, and 21 – Thompson in view of Farachi

Claims 1, 3, 4, 8, 12-14, 17, 20, and 21 stand rejected under 35 U.S.C. §103(a) as being obvious given Thompson in view of Farachi. The Examiner states that Thompson shows a microparticle preparation where a peptide bioactive is dispersed within a polyester matrix that is suitable for injection. [Office Action, P. 9.] The Examiner acknowledges that Thompson fails to show use of polyethylene sebacate as the polyester. [Office Action, P.10.] However, the Examiner states that Farachi shows biodegradable polyesters and polyalkylene sebacates. The Examiner further states that it would have been obvious to a person of ordinary skill in the art at the time of the invention to combine Thompsons and Farachi in the direction of claims 1, 3, 4, 8, 12-14, 17, 20, and 21.

Thompson appears to show microparticle compositions containing peptides and methods of preparing the compositions. [Thompson, Col. 1, lines 8-12.] Farachi appears to show a method for producing biodegradable aliphatic polyesters. [Farachi, Col. 1, lines 7-10.] Farachi appears to show a process for synthesizing poly(alkylene sebacates). [Farachi, Col. 2, lines 63-65.]

However, the combination of Thompson and Farachi fails to show use of poly(ethylene sebacate) or any other material that is *hydrolytically stable* or is adapted to degrade to *release a water-insoluble acid*. Moreover, Assignee also submits that the combination of Thompson and Farachi is improper in accordance with the 2010 KSR Guidelines Update because the combination would result in numerous unexpected and unpredictable advantages, as discussed previously above.

Claim 1 therefore distinguishes Thompson and Farachi. Claims 2-4, 6-8, 10-17, 19, 22, and 23 depend, directly or indirectly (e.g., through claim dependencies) from claim 1 and therefore also distinguish Thompson and Farachi for at least the same reasons as those discussed above with respect to claim 1. Claims 20 and 21 contain limitations similar to those of claim 1 and therefore also distinguish Thompson in view of Farachi for reasons similar to those discussed above with respect to claim 1.

Claims 1 and 7 – Duan in view of Nakumura and Burns

Claims 1 and 7 stand rejected under 35 U.S.C. §103(a) as being obvious given Duan in view of Nakumura and Burns. The Examiner states that Duan shows a composition composed of a particulate (granule) drug and a dispersing agent that is a compound comprising a chain of diol/diacid condensate and a propellant. [Office Action, P. 11.] The Examiner also states that Duan shows that the particulate drug can be coasted with a dispersant. [Office Action, P. 11.] The Examiner further notes that Duan does not show that the diacid is sebacic acid. However, the Examiner states that Nakamura shows use of polyethylene sebacate as a dispersing aid. The Examiner also states that Burns shows use of microspheres composed of polymers and that polyethylene is a polymer

contemplated in the particles. [Office Action, P. 11.] The Examiner further states that it would have been obvious to a person of ordinary skill in the art at the time of the invention to combine Duan, Nakamura and Burns in the direction of claims 1 and 7.

As discussed above, claims 1 and 7 distinguish Burns. Duan and Nakamura do not make up for the deficiencies of Burns. For example, Duan appears to show an *aerosol* drug formulation where the drug is dispersed through the air, e.g., a gas. [Duan, P. 1, lines 10-12.] Claim 1, on the other hand, recites a pharmaceutical composition that is in the form of one or more *solid or liquid drug delivery systems.* Assignee notes that the *aerosol* drug formulation of Duan is not a *solid or liquid drug delivery system.*

Nakamura appears to show a dispersing aid for dispersing a component, where the dispersing aid may be polyethylene sebacate. [Nakamura, Col. 7, ln. 41 – col. 8, ln. 17.]

However, Assignee submits that the combination of Duan, Nakamura, and Burns is improper in accordance with the 2010 KSR Guidelines Update because it would result in unexpected and unpredictable advantages, as discussed above. Moreover, the combination of Duan, Nakamura, and Burns fail to show use of poly(ethylene sebacate) in a combination that provides advantages such as the combination being *hydrolytically stable* or being capable of degrading to *release a water-insoluble acid.*

Claims 1 and 7 therefore distinguish Duan, Nakamura, and Burns.

New claims 22 and 23

New claims 22 and 23 depend from independent claim 1 and therefore distinguish the cited documents for at least the same reasons as those discussed above with respect

to claim 1. Moreover, new claims 22 and 23 contain limitations to further distinguish the cited documents.

Claim 22 recites "the pharmaceutical composition as claimed in claim 1, wherein said poly(ethylene sebacate) is capable of releasing *said water-insoluble acid without an addition of an external lipase to said at least one pharmaceutically active ingredient.*" Assignee notes that this limitation is not shown in any of the cited documents. Assignee notes that in accordance with claim 22, the pharmaceutical composition may degrade/metabolize in a manner similar to that of a fat in a patient's body, and therefore would not require use of an *external lipase.*

Claim 23 recites "the pharmaceutical composition as claimed in claim 1, wherein said pharmaceutical composition *comprises sebacic acid formed during hydrolysis of said poly(ethylene sebacate).*" Assignee notes that this limitation is not shown in any of the cited documents. Assignee notes that acidity of sebacic acid is much lower than that of monomers used in other pharmaceutical compositions. The acidity is lower as a result of its high molecular weight per unit of carboxylic acid, thus resulting in good tissue tolerance. Moreover, sebacic acid is not an irritant to tissue, unlike lactic acid or glycolic acid released by PLA or PGA compositions.

Even under the PTO guidelines and the KSR Guidelines update released after the KSR decision, as discussed above, the Examiner should explain how the applied documents are legally relevant despite limitations not being shown. Accordingly, Assignee respectfully submits that claims 1-4, 6-8, 10-17, and 19-23 are not made obvious by the

applied documents and requests withdrawal of the rejection of claims 1-4, 6-8, 10-17, and 19-21 under 35 USC § 103 (a).

Failure of the Assignee to respond to a position taken by the Examiner is not an indication of acceptance or acquiescence of the Examiner's position. It is believed that the Examiner's positions are rendered moot by the foregoing and, therefore, it is not necessary to respond to every position taken by the Examiner with which Assignee does not agree in this or other correspondence. Instead, it is believed that the foregoing addresses the issues raised by the Examiner and that the present claims are in condition for allowance.

CONCLUSION

The foregoing is submitted as a full and complete response to the Office Action mailed October 1, 2010. In view of the foregoing amendment and remarks, Assignee respectfully submits that pending claims are in condition for allowance and a notification of such allowance is respectfully requested.

If the Examiner believes that there are any remaining informalities that can be corrected by an Examiner's amendment, a telephone call to the undersigned at 503.439.6500 is respectfully solicited.

In the event there are any errors with respect to the fees for this response or any other papers related to this response, the Director is hereby given permission to charge any shortages and credit any overcharges of any fees required for this submission to Deposit Account No. 50-3130.

Respectfully submitted,

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/ James Wakely /
James Wakely, Patent Attorney
Registration No. 48,597

Customer No. 43831
Berkeley Law and Technology Group, LLP
17933 NW Evergreen Parkway, Suite 250
Beaverton, OR 97006
503-439-6500